

REMARKS

Applicants have carefully considered the Examiner's Non-Final Office Action, and respectfully request reconsideration of this Application in view of the above Amendment and the following remarks.

Pending in this Application are Claims 1, 5-8, 10, 12, 13, 76, 80-83, 85, 87, 88 and 137-139. Claims 137 and 139 have been amended.

Claims 13 and 88 have been amended to read "final third of gestation" instead of "third trimester of gestation" to account for the fact that mammals have varying lengths of gestation.

Claim 139 has been amended to read "female mammal" instead of "female pig or rat" in order to make the claim language consistent with the other claims.

I. PROVISIONAL REJECTIONS ON THE GROUNDS OF NONSTATUTORY OBVIOUSNESS-TYPE DOUBLE PATENTING

The Examiner has newly provisionally rejected Claims 1, 5-8, 10, 12, 13, 76, 80-83, 85, 87, 88, and 137-139 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over Claims 21-23 of U.S. Patent No. 6, 423,693 ("the '693 Patent"), in view of U.S. Patent No. 6, 551,996 ("the '996 Patent" or "Schwartz et al.").

The Examiner is of the opinion that it would have been obvious to one of ordinary skill in the art at the time of the invention to use the promoter of the '996 Patent in the method described in the '693 Patent for delivering to muscle cells *in vivo* an expression vector encoding growth hormone releasing hormone ("GHRH") for livestock improvement. Further, the Examiner has stated that the combined references render obvious all of the active method steps claimed in the current application, and that the functional effects of the method steps are considered to be inherent.

Applicants respectfully submit that the pending claims are neither obvious in view of, nor inherently present in, the combined references as suggested by the Examiner.

As the Examiner has noted, it was neither known at the time of the invention, nor suggested in the cited references, that combining the promoter of the '996 Patent with the method of the '693 Patent would result in weight changes *in the offspring* of a treated animal. Although the '996 Patent teaches that the SPc5-12 promoter has greatly increased transcriptional potencies when compared to natural muscle-specific promoters, the impact of this property on the improvement of weight in the offspring of an animal treated with the resulting vector was not predictable. At the time of the present application, the length of expression (which was driven by the muscle synthetic specific promoter SPc5-12) after a plasmid was injected intra-muscularly into a large mammal was not known, nor was the pattern of expression of the plasmid, the optimum dose needed, or level of expression over time. Furthermore, the effects of the said expression on the offspring of the treated animal were not even theoretically envisioned, regardless of plasmid construct elements.

The Examiner's suggestion that the properties of the methods for improving weight in offspring claimed in the current application are inherent in the combination of the previously disclosed vector and method for introducing a DNA vector to a cell does not form a basis for arguing that this method would be obvious to one of ordinary skill in the art as a way of improving weight in offspring.

Obviousness cannot be based on a finding that the properties of a novel composition are inherent in the combination of its ingredients. *In re Henderson*, 146 U.S.P.Q. 372, 375-76 (C.C.P.A. 1965) and *In re Gruskin*, 110 U.S.P.Q. 288, 292 (C.C.P.A. 1956).

In *Henderson*, the applicant claimed a new gasoline composition made up of known substances. Briefly, the gasoline composition contained the base gasolines and ether additives blended therein to produce decreased sensitivity in the gasoline composition. The claims were rejected by the patent examiner, and the Board of Appeals affirmed the examiner's rejection.

This was subsequently reversed by the Court. The Court noted that none of the references relied upon by the Patent Office provide the slightest teaching to one of ordinary skill in this art as to what might happen to the sensitivity factor in a gasoline composition consisting of such ethers with such base gasolines. The Court, in discussing the issue of "inherency," continued:

We are not impressed by the board's view, here urged by the solicitor, that because the ether additives would "inherently function" to produce the decreased sensitivity, the claimed blends are therefore obvious. Indeed, can it not be said that all functions of a substance are "inherent"? The fact remains that appellant has discovered that when certain ethers are blended with certain gasolines, the sensitivity of the resulting gasoline composition is less than the sensitivity of either the ether or the gasoline alone. The mere notion that such discovery would "flow naturally" from what appellant did does not mean that the discovery could be predicted from what the art had done. [Emphasis added].

Henderson at 375.

Similarly, the current application describes the unexpected result that when certain elements are combined in the claimed methods, the weight of the offspring of a treated animal can be impacted. Retrospective observation that these properties were inherently present in the elements combined does not mean that the discovery could have been predicted from what was known at the time of the invention.

In *Gruskin*, the applicant appealed the rejection of claims relating to a dentifrice composition containing a small amount of water-soluble chlorophyll and an inorganic salt of low solubility which has both an abrasive and an acid-neutralizing quality. In reversing the Board of Appeals' decision affirming the examiner's rejection, the Court, addressing the issue of "inherency," stated:

Thus while the references teach the use of a combination antacid-abrasive, the use of antiseptics in toothpaste, that water-soluble chlorophyll is a healing agent, and that diseased mouth tissue is acidic, there is no teaching in the references that the acid environment produced by diseased mouth tissue will cause water-soluble chlorophyll to lose its therapeutic effectiveness. We are therefore of the opinion that there is nothing in the references which would have suggested to one skilled in the art that the above teachings could have been combined to give appellant's toothpaste in spite of the fact that the actual substances disclosed in the references, if combined, inherently give a toothpaste having the characteristics of appellant's toothpaste. Thus it is our opinion that the references were improperly combined, and that the rejection based on the combination is erroneous. [Emphasis added.]

Gruskin at 292.

Thus, although several known substances may, if combined, inherently have certain properties that is not evidence that it would be obvious to one skilled in the art to make that

combination. In the current application, the mere possibility that the vector of the '996 Patent could be operatively linked to a DNA fragment and subsequently introduced to a cell using the method of the '693 Patent in no way suggests that the result of this process would manifest itself in the offspring of the treated animal.

Similarly, in *In re Adams*, 148 U.S.P.Q. 742 (C.C.P.A. 1966), the Court, in reversing the Patent Office's rejection of claims, had this to say about inherency and obviousness:

The Patent Office presents a number of hindsight arguments. It says Adams was not the first to use foam for heat transfer as fire departments and fire extinguisher users have been squirting foam on fires for years and housewives have been pouring aerated hot water on cold plates in the kitchen sink for years, in both of which operations heat transfer is *inherent*. Of course it is inherent, otherwise appellant's invention would not work. But patentability here does not hinge on inherency. It depends on the unexpected and unsuggested increase in heat transfer efficiency. No reference suggesting this has been produced, only ex post facto explanations as to why anyone should have been able to see that it would be more efficient to use aerated water. [Original italics, underline added.]

Adams at 745-46.

The outcome of treating a pregnant woman with any type of pharmaceutical product, including small molecules, gene therapies, and vaccines, is widely acknowledged to be unpredictable. Numerous pharmaceutical products have been used in pregnant women with unforeseen and sometimes highly undesirable outcomes in their offspring. This was the case with the use of the drug thalidomide to treat nausea in pregnant women in the 1950's and 1960's. Although it was not known at the time the drug was prescribed, thalidomide was later shown to have teratogenic effects in the children born to these women.

Similarly, the effect of treating a female animal according to the method of the current invention could not have been predicted based on what was known in the art at the time of the invention, and therefore cannot be considered to be unpatentable based on inherency.

This is further demonstrated in *In re Rijckaert*, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993), where the Federal Circuit has stated:

"The mere fact that a certain thing may result from a given set of circumstances is not sufficient [to establish inherency.]" *In re Oelrich*, 666 F.2d 578, 581-82, 212

USPQ 323, 326 (CCPA 1981)(emphasis in the original). “That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.” *In re Spormann*, 363 F.2d 444, 448, 150 USPQ 449, 452 (CCPA 1966). Such a retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection. See *In re Newell*, 891, 901, 13 USPQ2d 1248, 1250 (Fed.Cir. 1989).

In summary, to the extent that properties inherent in the prior art are unknown and unappreciated, they can suggest nothing. Applicants respectfully submit that the Examiner’s reasoning that the method steps for improving weight in offspring described in the current application are inherent in the claims of the cited references and therefore obvious, is incorrect. Previous to this application, the outcome of such a method was by no means predictable, nor known in the art.

II. REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

The Examiner has rejected Claims 1, 5-8, 10, 12, 13, 76, 80-83, 85, 87, 88, 137-139 in modified form under 35 U.S.C. §112, first paragraph, on the grounds that the specification is not enabling for the disclosed invention.

Specifically, the Examiner is of the opinion that, while the specification provides enablement for a method of improving or enhancing weight gain in an offspring from a female mammal, the specification does not reasonably provide enablement for a method of improving or enhancing growth in an offspring from a female mammal.

Applicants wish to respectfully point out that the Examiner has accepted the term “growth” in association with the instant invention in two previous Office Actions.

The Examiner stated on page 2 of the Office Action dated February 23, 2006, that

“...the specification, while being enabling for a method of improving or enhancing growth in an offspring from a female pig or rat comprising electroporating an effective amount of a vector into muscle cells by direct injection of the female pig or rat prior to or during gestation of the offspring, wherein the vector is comprised of a nucleic acid sequence encoding SEQ ID NO. 1 or SEQ ID NO. 8, wherein the nucleic acid sequence is operably linked to a hGH3’ untranslated region and a eukaryotic promoter, wherein said nucleic acid sequence is expressed in

the female and wherein the expression of said nucleotide sequence results in improved or enhanced growth or rate of growth of the offspring, and wherein the vector is a plasmid, does not reasonably provide enablement for...”

The Examiner has stated on page 3 of the Office Action dated August 9, 2005, that:

“...the specification, while being enabling for a method of improving or enhancing growth in an offspring from a female pig or rat comprising introducing an effective amount of a vector into muscle cells by intramuscular injection of the female pig or rat prior to or during gestation of the offspring, wherein the vector is comprised of a nucleic acid sequence encoding SEQ ID NO. 1 or SEQ ID NO. 8, wherein the nucleic acid sequence is operably linked to a hGH3’ untranslated region, wherein said nucleotide sequence is expressed in the female and wherein the expression of said nucleotide sequence results in improved or enhanced growth or rate of growth of the offspring, and wherein the vector is not a viral vector...”

Nevertheless, the claims have been amended to read “a method of improving or enhancing weight gain and development” based on the Examiner’s opinion. This terminology finds support in the specification where it is stated that in addition to having higher birth weights (please see specification, Examples 14, 15, and 21), the offspring of treated females had changes in hormonal profile in early development (please see paragraph 159, and Tables 6-12), changes in body composition (please see specification, paragraphs 144 and 147), and changes in other biochemical and hormonal parameters (please see specification, paragraph 152, and Tables 6 - 12). Applicants submit that these factors comprehend more than simply “weight”, and respectfully request that the Examiner allow these terms.

III. REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

The Examiner has newly rejected Claims 137 and 139 under 35 U.S.C. §112, second paragraph, on the grounds that they are indefinite and fail to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention.

The Examiner has pointed out that Claim 137 recites the limitation “vector” in Claim 1, and states that there is insufficient antecedent basis for this limitation in the claim. In response,

Applicants have amended Claim 137 to read: “The method of Claim 1, wherein the vector is formulated with a liposome, a cationic lipid, a polypeptide, or a combination thereof.”

The Examiner has further pointed out that Claim 139, line 4, appears to be missing an indefinite article.

In response, the claim has been amended to read:

“A method of improving or enhancing growth in an offspring from a female mammal comprising:

introducing an effective amount of a vector into muscle cells of the female mammal prior to or during gestation of the offspring, wherein the vector is comprised of a nucleic acid sequence encoding SEQ ID NO.1 or SEQ ID No. 8, wherein the nucleic acid sequence is operably linked to a eukaryotic promoter and to a hGH3' untranslated region, wherein said nucleotide sequence is expressed in the female mammal and wherein the expression of said nucleotide sequence results in improved or enhanced growth or rate of growth of the offspring, and wherein the vector is a plasmid.”

Thus, this amendment should render the Examiner's rejections based on the Second Paragraph of 112 moot.

IV. REJECTIONS UNDER 35 U.S.C. §102

The Examiner has newly rejected Claims 1, 5-8, 10, 12, 13, 76, 80-83, 85, 87, 88, and 137-139 under 35 U.S.C. §102(e) on the grounds that they are anticipated by U.S. Patent No. 6,551,996 to Schwartz et al. (“Schwartz et al.” or “the ‘996 Patent”) as evidenced by Aihara et al., 1998, Nature Biotech., 16:867-870 (“Aihara et al.”). Specifically, the Examiner has stated that the claimed methods of the current invention are considered to be inherent in the method steps taught by Schwartz et al.

As the Examiner has noted, Schwartz et al. does not teach or suggest a method for improving the weight of the offspring of a treated animal. However, the Examiner has argued that the alterations in weight of the offspring are inherent in the method described in Schwartz et al. We respectfully traverse this argument.

A. 35 USC §102 INHERENCY

In *International Nickel Co. v. Ford Motor Co.*, 119 U.S.P.Q. 72 (SDNY 1958), the Court held that, in determining anticipation, the focus is on the question of whether the unintended production of a product was **purely a matter of chance** (*i.e. was sporadic*) or was the **inevitable result** of the reference teaching. In *Continental Can Company USA, Inc. v. Monsanto Co.*, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991), the Federal Circuit held that anticipation under the inherency doctrine requires that the missing descriptive matter be “**necessarily present** in the thing described in the reference [Emphasis added].”

To establish anticipation through inherency, the claim limitation must be “necessarily present” within the cited reference. *See Crown Operations*, 62 U.S.P.Q.2d at 1923. The mere fact that a certain claim limitation *may* result from a given set of circumstances in a prior art reference is not sufficient. *See Rapoport v. Dement*, 59 U.S.P.Q.2d 1215, 1222 (Fed. Cir. 2001). In *Rapoport*, the alleged infringer, who was attempting to invalidate the patent, did not demonstrate that the claimed subject matter would “necessarily result” from the treatment given in the reference. *See id.* He only argued that the preferred treatment in the reference did not exclude the claimed subject matter. *See id.* The court upheld the BPAI’s decision that the reference did not disclose the claimed subject matter and did not anticipate the claim. *See id.* at 1223.

Further, a prior art reference cannot inherently disclose a claim element, thereby anticipating that element, unless the prior art reference contains an enabling disclosure. Inherency may not be assumed based solely on similarities between the claimed invention and the prior art. *See Crown Operations Int’l Ltd. v. Solutia, Inc.*, 62 U.S.P.Q.2d 1917, 1923 (Fed. Cir. 2002). Although one of ordinary skill in the art is not required to recognize the inherency in the prior art, the Federal Circuit requires that the assertedly anticipating disclosure must enable the subject matter of the reference and thus of the patented invention without undue experimentation. *See Elan Pharmaceuticals, Inc. v. Mayo Foundation for Medical Education & Research*, 68 U.S.P.Q.2d 1373, 1374 (Fed. Cir. 2003). In other words, to serve as an anticipating reference, the reference must enable that which it is asserted to anticipate. *See id.* at 1375 – 76; *see also Toro Co. v. Deere & Co.*, 69 U.S.P.Q.2d 1584, 1590 (Fed. Cir. 2004) (reiterating that

inherent anticipation by a prior-art embodiment is not possible unless that embodiment is itself sufficiently described and enabled).

Thus, in addition to the requirement of “necessarily present” within the cited reference, anticipation under the inherency doctrine also requires that the prior-art embodiment is (1) sufficiently described; and (2) enabled.

Applicants respectfully submit that Schwartz et al. as evidenced by Aihara et al., cannot anticipate the pending claims under §102 inherency because the prior-art embodiment in Schwartz et al. and in Aihara et al. is NOT sufficiently described and is NOT enabled. Further, the unintended production of product is NOT the inevitable result of the teaching of the reference.

The law is clear that in order to anticipate, there must be no difference between the claimed invention and the reference disclosure, as viewed by person of ordinary skill in the field of the invention. *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 18 U.S.P.Q. 1001, 1010 (Fed. Cir. 1991). When a claimed invention is not identically disclosed in a reference, and instead requires picking and choosing among a number of different options disclosed by the reference, then the reference does not anticipate. *Mendenhall v. Astec Industries, Inc.*, 13 U.S.P.Q. 2d 1913, 1928 (Tenn. 1988), *aff'd*, 13 U.S.P.Q.2d 1956 (Fed. Cir. 1989).

1. The Requirement of Impermissible Hindsight Picking and Choosing

Schwartz et al. is silent about using intramuscular electroporation to introduce a vector into an animal. The Examiner then replied upon the teaching of Aihara et al. to “fill in this gap” of intramuscular electroporation.

In order to come up with what is claimed here, the Examiner is selectively choosing the disclosure of intramuscular electroporation in Aihara et al., but ignoring its total teaching of using a vector of IL-5 transgene controlled by a CAG promoter. In contrast, the present invention requires the case of a vector which is capable of expressing a GHRH or protein analog thereof. Here the Examiner is selectively choosing the teaching of Schwartz et al. of using SPc5-12 promoter, but ignoring the total teaching of Schwartz et al. in that the weight of the treated animals were increased. Unlike the present invention, Schwartz et al. did not make any selection

of treating only female animals, nor describe or teach that effects are in fact on the treated subject's offspring, and NOT on the treated subject itself.

As discussed above, when a claimed invention is not identically disclosed in a reference, and instead requires picking and choosing among a number of different options disclosed by the reference, then the reference **does not anticipate**. *Mendenhall v. Astec Industries, Inc.*, *id.*

2. Prior Art Embodiment is Not Sufficiently Described

Although Schwartz et al. teaches that the SPc5-12 promoter has greatly increased transcriptional potencies when compared to natural muscle-specific promoters, the impact of this property on the improvement of weight in the offspring of an animal treated with the resulting vector is unpredictable. The teachings of Schwartz et al. only include information on appropriate dosages of DNA for treating porcine animals, and not the female animals which are claimed in this application. Schwartz et al. describes a method for improving the weight of the treated animal only, without suggestion of any effect on animals aside from the treated animal. Schwartz et al. is silent on introducing the plasmid into the muscle of a recipient via electroporation.

The vector described in Aihara et al. is the IL-5 transgene controlled by a CAG promoter. The CAG promoter consists of a cytomegalovirus (CMV) immediate-early enhancer, a chicken beta-actin transcription start site and a rabbit beta-globin intron. As shown in Figure 2 of the reference of Aihara et al., transgene expression using this vector is substantially decreased at day 21 to levels similar to background, and is virtually undetectable by day 42. This duration of transgene expression would not be sufficient to result in the physiological effects on the offspring of the treated animals described in the present application

As such, neither Schwartz et al. nor Aihara et al. includes all details necessary to invariably reproduce the currently claimed invention, and, therefore, even in combination, they cannot be used as a basis for anticipation under inherency.

3. Prior Art Embodiment is Not Enabled

Aihara et al. describes a method for introducing DNA to cells which comprises an electroporation array that consists of a pair of stainless steel needles 5 mm in length, 0.4 mm in diameter, and fixed with a distance (gap between them at 3 or 5 mm). This type of array would be completely inappropriate for electroporating the muscles of a large mammal (pig, cow, horse, or the like) in view of the fact that even the most superficial muscles of larger mammals are covered by relatively thick skin and a layer of subcutaneous fat and fascia. An electroporation array such as the one described in the Aihara et al. would not be expected to penetrate the muscles of a larger mammal or to deliver an efficient electroporation sequence. Moreover, if the electrodes were capable of penetrating the skin and fat layers, the arrangement of the array described by Aihara et al. would not accommodate the volume and dose of plasmid formulation that would be required for this method when practiced in a larger mammal when used in accordance with the method of Schwartz et al.

In addition, as discussed above, the vector described in Aihara et al. is the IL-5 transgene controlled by a CAG promoter. The CAG promoter consists of a cytomegalovirus (CMV) immediate-early enhancer, a chicken beta-actin transcription start site and a rabbit beta-globin intron. As shown in Figure 2 of the reference of Aihara et al., transgene expression using this vector is substantially decreased at day 21 to levels similar to background, and is virtually undetectable by day 42. This duration of transgene expression would not be sufficient to result in the physiological effects on the offspring of the treated animals described in the present application.

Thus, prior art embodiment of Aihara et al. is not an enabling disclosure.

4. The Unintended Production of Product is Not the Inevitable Result of the Teaching of the References

Both Schwartz et al. and Aihara et al. disclose treating animals in general, not specifically females or males. It is a known fact that both males and females can have offspring. Yet improving weight and growth in offspring occur only when female animals were treated with the plasmids and methods of the present invention. Thus, it cannot be said that the unintended

production of “increased weight and growth in offspring” is an inevitable result of the teaching of the two cited references which do not make any distinction between males and females.

Applicants therefore respectfully submit that none of the requirements for anticipation under inherency is present in either of the cited references, or in their combination. Moreover, hindsight selective choosing and picking are required to come up with the claimed invention.

B. PRIMA FACIE OBVIOUSNESS

The Examiner has further asserted that the methods claimed in the current application are obvious in light of the teachings of Schwartz et al. in view of the Aihara et. al. Applicants respectfully disagree on the following grounds.

1. The Requirement of Impermissible Hindsight Picking and Choosing

This discussion has been presented above.

2. Unexpected Results

Applicants respectfully submit that the current application describes unexpected advantages in applying a method to female animal in order to produce a result in her offspring. It does not follow from the disclosure of Schwartz et al. that each time the method is practiced it would result in offspring with improved weight. In order for this to be the case, the method would always have to be practiced in a female animal. Applicants therefore respectfully submit that the outcome of improving weight in the offspring of treated animals is not necessarily present in the teachings of Schwartz et al. These unexpected advantages were not described or suggested in the teachings of the cited reference.

In *Lindemann Maschinenfabrik GmbH v. American hoist and Derrick Co.*, 730 F.2d 1452, 221 U.S.P.Q. 481 (Fed. Cir. 1984), the Court held that:

The fact that a patent specifically discloses and claims a combination of features previously used in two separate devices is not fatal to patentability. A basic issue is whether applied references, alone or in any combination, suggest the claimed invention as a solution to the specific problem solved. The claimed invention achieved new and unexpected results nowhere suggested in the prior art, and that

achievement was overlooked. The district court erroneously focused its inquiry 'solely on the product created, rather than on the obviousness or non-obviousness of it creation.' The initial inquiry should be directed to the vantage point of attacking the problem solved by the invention at the time the invention was made. When prior art itself does not suggest or render obvious the claimed solution to that problem, the art involved does not satisfy the criteria of the 35 U.S.C. §103 for precluding patentability.

3. Against Conventional Wisdom

Further, to use the method described in Schwartz et al. on a female animal as claimed in this application is against conventional wisdom. As discussed above, previous experience with treating females with pharmaceutical agents has resulted in widely variable results in offspring, and it cannot be relied upon that the same or similar results will be observed in the offspring as were observed in the originally treated animal. This unpredictable nature illustrates that what was known in the field at the time of the invention did not point toward carrying out these experiments.

4. Obvious to Try

Finally, simply because it may be desirable to try using variations of starting materials or specific conditions in each of the steps of a known method does not satisfy the standard for §103 obviousness. "Disregard for the unobviousness of the results of 'obvious to try' experiments disregards the 'invention as a whole' concept of §103" *In re Antonie*, 559 F.2d 618, 620, 195 U.S.P.Q. 6, 8 (C.C.P.A. 1977). "Further, in the determination for obviousness, the intended purpose of a claimed invention, particularly in regard to the problem solved by the invention, must be considered. Such consideration is part 'of the whole.'" *In re Wright*, 6 U.S.P.Q.2d 1959 (Fed. Cir. 1988).

In short, Applicants respectfully submit that the combination of Schwartz et al. with Aihara et al. would not have rendered the claimed invention obvious.

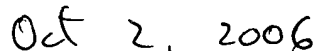
V. **CONCLUSIONS**

Applicants respectfully submit that, in light of the foregoing amendments and argument, Claims 1, 5-8, 10,12, 13, 76, 80-83, 85, 87, 88 and 137-139 are in condition for allowance. A Notice of Allowance is therefore requested.

Respectfully submitted,



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